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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
08/908,884	08/08/97	DONG	X	00786/33904

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EXAMINER	
NELSON, A	
ART UNIT	**PAPER NUMBER**
1649	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/908,884	Applicant(s) Xinnian Dong, et al.
	Examiner Amy Nelson	Group Art Unit 1649

☒ Responsive to communication(s) filed on *8/8/97 and 9/28/98* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-46* is/are pending in the application.

Of the above, claim(s) *30-35, 37-39, and 43-46* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-29, 36, and 40-42* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3 & 7*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, Claims 1-29, 36 and 40-42, in Paper No. 8, filed 9/28/98, is acknowledged.

2. Claims 30-35, 37-39, and 43-46 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

3. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

5. The Database Search Reports filed in the Information Disclosure Statement filed 9/28/98 have been considered, but are not suitable for publication with the patent document.

Specification

6. This application is informal in the arrangement of the specification. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(i) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing (see 37 CFR 1.821-1.825).

In particular, Applicant should amend the Specification to insert the following subheadings:

--BRIEF DESCRIPTION OF THE DRAWINGS-- and --DETAILED DESCRIPTION OF THE INVENTION--.

Claim Objections

7. Claims 13-29, 36, and 40-42 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n).

Amendment of Claims 13-17, 22, 36 and 40 to recite --any one of claims-- would obviate this objection.

8. Claims 17-29 and 36 are objected to because of the following informalities:

At Claim 17, line 1, "an isolated nucleic acid molecule" should be changed to --the isolated nucleic acid molecule-- as it refers to a previous claim.

At Claim 22, line 1, "a nucleic acid molecule" should be changed to --the nucleic acid molecule-- because it refers to a previous claim.

At Claim 28 and 29, "a transgenic plant" should be changed to --the transgenic plant-- because it refers to a previous claim.

At Claim 36, line 3, "a nucleic acid molecule" should be changed to --the nucleic acid molecule-- because it refers to a previous claim.

At Claim 36, line 3, the semi-colon should be changed to a comma.

Claim Rejections - 35 USC § 112

9. Claims 1-29, 36 and 40-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is drawn broadly toward isolated nucleic acid molecules encoding an acquired resistance polypeptide. Applicant has described the composition and structure of a single genomic clone (and its respective cDNA clone) from *Arabidopsis* which encodes an acquired resistance polypeptide. Applicant does not describe the composition or structure of any other isolated nucleic acid molecules which definitively encode an acquired resistance polypeptide, and hence it is not clear from the instant specification that the Applicant was in possession of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

10. Claims 1-29, 36, and 40-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to an isolated *Arabidopsis* DNA molecule that encodes the acquired resistance polypeptide of SEQ ID NO:14, a vector, transformed host cell, and transgenic plant comprising said DNA molecule, and methods of producing an acquired resistance polypeptide in a host cell and of providing increased disease resistance in a transgenic

plant with said DNA molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant claims an isolated nucleic acid molecule encoding an acquired resistance polypeptide, a vector, transformed cell, and transgenic plant comprising said DNA molecule, and methods of producing an acquired resistance polypeptide in a cell and of providing increased disease resistance in a transgenic plant with said nucleic acid molecule.

Applicant teaches transformation of *Arabidopsis* with the reporter construct BGL2-GUS, mutagenization of the transformed plants, followed by screening of the mutagenized plants to identify mutants that fail to express the reporter construct in the presence of SA and INA (Fig. 2). Applicant teaches that the mutants also lack enhanced PR gene expression in response to SA, INA or normally virulent pathogens. Applicant teaches map-based positional cloning of the *NPR1* gene from *Arabidopsis* (Fig. 4, SEQ ID NO:1, encodes SEQ ID NO:3), and teaches screening of a cDNA library to isolate the respective cDNA clone (Fig. 5, SEQ ID NO:2, encodes SEQ ID NO:3). Also, Applicant teaches functional complementation of mutant *Arabidopsis* plants with a construct comprising the CaMV 35S promoter operably linked to the *NPR1* cDNA, and teaches that wild type *Arabidopsis* plants transformed with the same construct show a good correlation between the level of expression of the introduced gene and increased resistance to the bacterial pathogen *Pseudomonas syringae* pv. *maculicola* and the fungal pathogen *Perenospora parasitica* (Fig. 9, Table 1). Finally, Applicant teaches isolation of a structurally related gene from *Nicotiana*

glutinosa by screening a cDNA library from TMV-infected plants (Fig. 7, SEQ ID NO:13, encodes SEQ ID NO:14).

Applicant does not teach an isolated nucleic acid molecule other than the *NPR1* gene from *Arabidopsis* which clearly functions in acquired resistance, nor does Applicant teach vectors, transformed cells, and transgenic plants comprising other nucleic acid molecules. Furthermore, Applicant does not teach a method of making an acquired resistance polypeptide with another nucleic acid molecule and in a cell other than in a host cell in culture, and Applicant does not teach a method of providing increased disease resistance in transgenic plants with another nucleic acid molecule.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

The state of the art for isolation of cDNA or genomic clones with a defined functionality is highly unpredictable. Significant guidance is required with regard to hybridization/ wash condtions or PCR reaction conditions that will allow specific isolation of the target genes. Applicant has characterized and isolated a single acquired resistance gene from *Arabidopsis,* and provided general guidance for hybridization and PCR techniques. Although Applicant describes isolation of

a structurally related gene from *Nicotiana glutinosa* by hybridization with the *NPR1* cDNA, the hybridization conditions are not high stringency (see Specification, p. 49, lines 18-20 as compared to the definition of high stringency at p. 51, lines 13-21), and Applicant does not provide any evidence to support the functional relatedness of the *Nicotiana* cDNA to the *NPR1* gene. The novelty of the instant invention is the isolation of a gene which plays a functional role in the acquired resistance response in plants. Applicant has not precisely defined the function of the *NPR1* gene, nor has Applicant provided any guidance with respect to the structural and functional similarity of related genes among different plant species. In the absence of such guidance, and in the absence of specific evidence regarding the functional role of the isolated *Nicotiana* cDNA or guidance with respect to hybridization/wash conditions which would allow specific isolation of nucleic acid molecules from other plant species which are functionally related to *NPR1*, undue trial and error experimentation would be required to screen through the vast number of cDNA and genomic clones from *Arabidopsis* or another plant species, to identify those that are functionally related to *NPR1* and also play a role in acquired resistance in plants.

Furthermore, Claim 36 reads on a method of producing an acquired resistance polypeptide in a cell *in vivo*, which in turn reads on gene therapy. Applicant has clearly not provided guidance for expression of an acquired resistance gene in a mammal, for example. The scope of the claims should be limited to the teachings of the specification, and hence should be limited to a host cell in culture.

When the *Wands* factors are weighed it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims, and therefore the invention is not enabled.

11. Claims 1-29, 36, and 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At Claim 1, line 1, the term "including" is indefinite because it is not known whether open or closed claim language is intended. The term should be changed to --consisting of--.

At Claim 1, line 2, Claims 10-12, lines 1-2, and Claim 36, line 1, the phrase "acquired resistance polypeptide" is indefinite. The phrase is not defined in the Specification, however Applicant defines "acquired resistance gene" to mean "a gene encoding a polypeptide capable of triggering a plant acquired resistance response (for example, a systemic acquired resistance (SAR) or local acquired resistance response (LAR)) in a plant cell or plant tissue" (Specification, p. 9, lines 2-25). However, it is not clear what is encompassed by a "plant acquired resistance response," whether it means increased pathogen resistance, increased PR gene expression, increased response to SA or INA, or some other response. SAR and LAR are complex phenomena in plants and involve a host of different signal transduction pathways, transcriptional regulatory mechanisms, and phenotypic effects. Many of the molecules and pathways involved in SAR and LAR also play roles in other plant devleopmental or biochemical pathways. Hence, it is

not known what responses, and hence what isolated nucleic acid molecules, are encompassed by the claims. Appropriate correction is required to more clearly define the metes and bounds of the claimed subject matter.

At Claim 1, lines 2-3, the phrase "is capable of conferring" is indefinite because it is unclear whether or not the polypeptide confers resistance. The phrase should be changed to --confers--.

At Claim 2, lines 1-2, the phrase "is capable of meditating" is indefinite because it is unclear whether or not the polypeptide mediates expression. Also it is not clear what is intended by the term "mediating." There are many different ways that expression could be mediated, *e.g.* in level of expression, time of expression, location of expression; and many different mechanisms for mediation, *e.g.* by binding of a polypeptide to the promoter region, by regulation of the transcriptional machinery, or by interference with translation or post-translational processing. Applicant has not clearly defined the term, and hence it is not known what is encompassed by the claim. Appropriate correction is required to clearly define the metes and bounds of the claimed invention.

At Claim 4, lines 4, the phrase "polypeptide is obtained from" does not make sense. The claim is directed to an isolated nucleic acid molecule, and hence it is the nucleic acid molecule not the polypeptide which is "obtained." It is recommended that the phrase be changed to --isolated nucleic acid molecule is from--.

At Claims 10-12, line 2, the term "that" is indefinite because it is not clear whether it refers to the nucleic acid molecule or the polypeptide. It is recommended that the term be changed to --and that--.

At Claims 10-12, line 2, the phrase "specifically hybridizes to" is indefinite. Applicant defines the phrase to mean "at least under low stringency conditions as described herein, and preferably under high stringency conditions, also as described herein" (Specification, p. 12, lines 1-3), and Applicant defines high and low stringency conditions (Specification, p. 51, line 13 - p. 52, line 3). The phrase is indefinite because it is not clear what is encompassed by the claim, *i.e.* those nucleic acid molecules which hybridize under low stringency conditions, or those which hybridize under high stringency conditions. In particular, the term "preferably" is a qualitative term and hence it is not known if high stringency conditions are required or not. Also, Applicant defines both high stringency and low stringency with two different sets of conditions, and also suggests that "other appropriate conditions may be determined by those skilled in the art." Hence, the stringency conditions are not clearly defined and it is not known what is encompassed by the claim. Appropriate correction is required to more clearly define the metes and bounds of the claimed subject matter.

At Claim 13, line 2, the term "mediates" is indefinite. There are many different ways that expression could be mediated, *e.g.* in level of expression, time of expression, location of expression; and many different mechanisms for mediation, *e.g.* by binding of a polypeptide to the promoter region, by regulation of the transcriptional machinery, or by interference with translation

or post-translational processing. Applicant has not clearly defined the term, and hence it is not known what is encompassed by the claim. Appropriate correction is required to clearly define the metes and bounds of the claimed invention.

At Claim 16, line 2, the phrase "being capable of directing expression" is indefinite because it is unclear whether or not the vector directs expression. The phrase should be changed to --directing expression--.

At Claims 17, 22, 36 and 40, "nucleic acid molecule of claim ... 16" lacks proper antecedent basis. Claim 16 is drawn to a vector, not a nucleic acid molecule. Appropriate correction is required.

At Claims 24 and 27, line 1, "said transgenic angiosperm" lacks proper antecedent basis. Appropriate correction is required.

At Claim 36, line 3, "providing a cell transformed with" is not an active method step. It is recommended that the method step be changed to recite --transforming a cell with--.

At Claim 36, line 4, the phrase "positioned for expression in the cell" is indefinite because Applicant has not defined how the nucleic acid molecule should be positioned for expression, and hence the phrase has no meaning. It is recommended that the phrase be changed to --to allow expression of the nucleic acid molecule in the cell--.

At Claim 36, line 5, the phrase "under conditions for expressing" is indefinite. Applicant has not defined what conditions would allow expression and hence the phrase has no meaning. It is recommended that the phrase be changed to --to express--.

At Claim 40, line 3, the term "including" is indefinite because it is not known whether open or closed claim language is intended. The term should be changed to --comprising--.

At Claim 40, line 4, "said nucleic acid" lacks proper antecedent basis and should be changed to --said nucleic acid molecule--.

At Claim 40, lines 4-5, "positioned for expression in the plant cell" is indefinite because Applicant has not defined how the nucleic acid molecule should be positioned for expression, and hence the phrase has no meaning. It is recommended that the phrase be changed to -- is expressed in the plant cell--.

At Claim 40, line 6, the term "growing" is unclear because the cell must divide as well as grow in order to produce a plant. It is recommended that the term be changed to --regenerating--.

Claim Rejections - 35 USC § 101

12. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 17-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims read on a naturally occurring cell, which is a product of nature, and not one of the five statutory categories of patentable subject matter. Amendment of the claims to insert --transformed-- would obviate this rejection.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

15. Claims 1, 2, 4-13, 15-29, 36, and 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Ryals *et al.* (WO 95/19443, 1995).

The claimed invention is indefinite for the reasons described *supra*. In particular, it is not known what is encompassed by "acquired resistance polypeptide." Moreover, it is not known what is encompassed by "specifically hybridizes." The claims are read broadly to mean an isolated nucleic acid molecule which encodes a polypeptide that induces any response characteristic of an SAR or LAR response, including enhanced pathogen resistance, and to said isolated nucleic acid molecules wherein said molecules hybridize to SEQ ID NO:1, 2 or 13 under low stringency conditions.

Ryals teaches isolated SAR nucleic acid molecules which encode polypeptides that enhance pathogen resistance (Abstract, p. 21-23). It is expected that the isolated nucleic molecules of Ryals would hybridize to SEQ ID NO:1, 2 or 13 under low stringency conditions. Ryals teaches methods of producing the encoded polypeptides in transformed plant cells, and of

enhancing disease resistance in transgenic plants by expressing the disclosed nucleic acid molecules, as well as transgenic plant cells, plants, and seeds thereby obtained (Abstract, p. 20-21, for example). Ryals teaches both cDNA and genomic DNA molecules (p. 8, for example), teaches nucleic acid molecules from tobacco (Solanaceae) and *Arabidopsis* (Cruciferae) (p. 8, Examples 1 and 3), and teaches DNA molecules involved in signal transduction and DNA/DNA interactions, and hence which presumbly regulate expression of pathogenesis-related polypeptides (p. 10, 14, for example). Ryals also teaches vectors comprising said nucleic acid molecules and expression control regions (p. 21, for example), and *Agrobacterium* comprising said nucleic acid molecules (p. 1-2, for example). Ryals teaches a variety of transgenic plants including tobacco (Solanaceae), and *Arabidopsis* (Cruciferae), wheat and maize (monocots) (p. 38, 43-45, for example), and teaches increased resistance to a variety of pathogens, including insects, nematodes, and *Perenospora* (p. 38, 46, for example). Therefore, all of the claim limitations have been previously disclosed by Ryals.

16. Claims 1-4, 6-24, 26, 28-29, 36, and 40-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhang *et al.* (U.S. Patent 5,623,054).

The claimed invention is indefinite for the reasons described *supra.* In particular, it is not known what is encompassed by "acquired resistance polypeptide." Moreover, it is not known what is encompassed by "specifically hybridizes." The claims are read broadly to mean an isolated nucleic acid molecule which encodes a polypeptide that induces any response characteristic of an

SAR or LAR response, including enhanced pathogen resistance, and to said isolated nucleic acid molecules wherein said molecules hybridize to SEQ ID NO:1, 2 or 13 under low stringency conditions.

Zhang discloses isolated nucleic acid molecules, both cDNA and genomic DNA, which encode a polypeptide involved in protecting plants from pathogens, and hence an acquired resistance polypeptide, from *Arabidopsis* (Cruciferae) (Abstract, col. 6-9). Moreover, the polypeptide of Zhang directly interacts with polypeptides involved in pathogen resistance, and it is expected that the polypeptide comprises an ankyrin repeat because it was isolated by a yeast trap sytem using an *Arabidopsis* ankyrin repeat protein as a bait (col. 6, lines 43-61). It is also expected that the isolated nucleic molecules of Zhang would hybridize to SEQ ID NO:1, 2 or 13 under low stringency conditions. Zhang also discloses vectors comprising the isolated nucleic acid molecules and expression control regions, host cells, including plant and *Agrobacterium* cells, transformed with said isolated nucleic acid molecules, and transgenic plants and seeds comprising said isolated nucleic acid molecules, specifically tobacco (Solanaceae) (col. 1, line 65 - col. 2, line 36; col. 18-20). Zhang also teaches a method of producing the encoded protein in a host cell (col. 13-17) and a method of enhancing resistance to bacteria, insects, nematodes, fungi and viruses by expression of the isolated nucleic acid molecule in transgenic plants (Abstract; col. 1, lines 32-45, col. 4, lines 36-42; col. 17-20).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 1-4, 6-29, 36, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang *et al.* (U.S. Patent 5,623,054).

The teachings of Zhang are discussed *supra*.

Zhang does not teach a transgenic plant that is cruciferous or a monocot. Zhang also does not teach a method of enhancing resistance to *Phytophthora, Perenospora or Pseudomonas*.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the invention of Zhang to produce other transgenic plants than the disclosed tobacco plants, including cruciferous plants or monocots, because that would allow enhancement of pathogen resistance in other plant species. Plant transformation techniques were well known to one of skill in the art at the time of Applicant's invention as disclosed by Zhang (col. 17-18), and it would have been obvious to substitute one plant species for another because different plant species are functional equivalents and it would have been obvious to substitute one functional equivalent for another. It also would have been obvious to modify the method of Zhang to enhance resistance to other plant pathogens including *Phytophthora*, *Perenospora* or *Pseudomonas*, because all of these are significant plant pathogens. The isolated nucleic acid

molecules of Zhang confer general pathogen resistance by mediating signal transduction events leading to enhanced plant defense mechanisms and hence would be expected to be effective against a wide variety of pathogens. One would have had a reasonable expectation of success in view of the success of Zhang.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy J. Nelson whose telephone number is (703) 306-3218. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Douglas Robinson, can be reached at (703) 308-2897. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Amy Nelson

Amy J. Nelson, Ph.D.

December 5, 1998